

REMARKS

In the last Office Action, the Examiner advised Applicants that if claim 20 is found allowable, claim 28 depending from claim 15 will be objected to under 37 CFR 1.75 as allegedly being a substantial duplicate thereof (potential double patenting objection) and rejected claims 15-20 and 23-29 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,010,475 to Thomas et al. (Thomas) in view of U.S. Patent No. 5,840,190 to Scholander et al. (Scholander).

By this Reply, Applicants propose to cancel claims 15-20 and 23-25 without prejudice, amend claims 26-29, and add new claim 30 to more appropriately define the present invention. Upon entry of this Amendment After Final, claims 26-30 will be pending in the above-captioned patent application. Prompt consideration of this Reply and allowance of the application are earnestly requested.

At the outset, Applicants note that proposed amended claim 26 recites, “sterilizing the exchanger once the semipermeable membrane based on polyacrylonitrile carrying anionic or anionizable groups is coated with the cationic polymer and the anticoagulant agent.” (Emphasis added.) Support for this change to claim 26 may be found in the specification, for example, at page 11, lines 15-19. In addition, proposed new claim 30 recites, among other things, that “sterilizing the exchanger further includes sterilizing the semipermeable membrane with gamma irradiation or with ethylene oxide.” Support for new claim 30, may be found in the specification, for example, at page 11, lines 4-6. These changes do not raise new issues and should allow for immediate examination by the Examiner.

Applicants respectfully traverse the Examiner’s assertion regarding double patenting objection (Office Action at 2), in which the Examiner asserted that “should

claim 20 be found allowable, claim 28 depending from claim 15 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.” (*Id.*) Applicants respectfully submit that the alleged double patenting is rendered moot by Applicants’ cancellation of both claims 15 and 20.

Applicants also respectfully traverse the Examiner’s rejection of claims 15-20 and 23-29 under 35 U.S.C. § 103(a) as being obvious over Thomas in view of Scholander. To the extent the Examiner’s rejection under 35 U.S.C. § 103(a) is understood, Applicants note that in order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references, when combined, must teach or suggest all the claim limitations. See M.P.E.P. § 2143. Applicants respectfully submit that the Examiner failed to establish a *prima facie* case of obviousness.

Applicants respectfully note that the Examiner’s rejection is moot with respect to cancelled claims 15-20 and 23-25. Insofar as the Examiner’s rejection under 35 U.S.C. § 103(a) is relevant to amended claims 26-29 and new claim 30, Applicants respectfully submit that amended claim 26, for example, is not obvious over Thomas in view of Scholander, because neither reference teaches nor suggests a method comprising the steps of “bringing [a cationic polymer] solution in contact with a semipermeable membrane” before “purging the exchanger of the [cationic polymer] solution,” and then “bringing a solution [containing an anticoagulant agent] in contact with the

semipermeable membrane” before “purging the exchanger of the solution [containing an anticoagulant agent],” and then “sterilizing the exchanger **once** the semipermeable membrane based on polyacrylonitrile carrying anionic or anionizable groups is **coated** with the cationic polymer and the anticoagulant agent.” (Emphasis added.)

Without identifying any particular portion of Thomas, the Examiner asserts that the reference teaches bringing a cationic polymer “solution in contact with the membrane and then purging the solution of cationic polymer.” (Office Action at 6.) However, Thomas teaches that “after deposition [of a drop] of the [cationic polymer] substance [on the membrane surface]...the apparatus can be sterilized.” (Col. 5, lines 44-46.) This sterilization occurs prior to purging “during which the blood compartment is rinsed and filled with a sterile aqueous solution.” (Col. 5, lines 50-51.) The circulation of the aqueous solution “starts from the access where the [polymer] substance has been deposited” (col. 3, lines 4-5) and only then, after sterilizing, is the membrane surface coated with “a durable molecular layer of the [polymer] substance.” (Col. 3, lines 7-8.) In fact, Thomas touts modifying the membrane surface after sterilization as an advantage of the disclosed process: “the surface modified by the substance is obtained only after sterilization of the apparatus, with the result that this modified, biocompatible surface does not run the risk of being damaged by a highly energetic sterilization.” (Col. 3, lines 35-40.)

The Examiner, however, cites column 8, lines 34-51, to allegedly show that “Thomas also teaches sterilizing the membrane with ethylene oxide after coating with PEI.” (Office Action at 4.) The Examiner acknowledges that the “steps of sterilizing after coating with PEI is described by Thomas as less desirable.” (*Id.*) However, the

Examiner then discounts this teaching in Thomas to assert that Thomas does not teach away from sterilization after coating a membrane surface with a cationic polymer.

Applicants disagree and note that Thomas must be viewed as a whole. It is improper for the Examiner to cite specific portions of the reference to misinterpret the teaching of the reference as a whole. Thomas does not merely state, as the Examiner suggests, that “sterilizing after coating is...less desirable.” Nor does Thomas provide a “broader disclosure” that would render the claimed invention obvious, as is present in In re Susi, cited by the Examiner. (Office Action at 4.) Thomas expressly teaches away from sterilizing the membrane after attaching PEI by reciting a list of extra steps to be carried out in order to make such sterilization possible. (Col. 8, lines 35-55.) In fact, Thomas clearly discloses that if a membrane “were to be treated with PEI before the sterilization of the dialyser, it would be necessary: 1-to deglycerinate the fibres by rinsing the dialyser with an aqueous solution; [and] 2-to circulate a solution of PEI through the blood compartment.” Moreover, these additional steps are quite different than those recited in amended claim 26, and therefore, this disclosure in Thomas would not render claim 26 obvious.

Further, the Examiner conceded that “Thomas does not teach the coating of the anticoagulant.” (Office Action at 6.) Thus, Thomas fails to teach or suggest sterilization after treating a semipermeable membrane with a cationic polymer solution, purging the same, and then treating a semipermeable membrane with a solution having an anticoagulant agent and then “purging the exchanger of the solution containing the anticoagulant agent,” as recited in amended claim 26. Nor does the Examiner suggest

that Thomas teaches “purging the exchanger of the solution containing the anticoagulant agent,” as recited in claim 26.

The Examiner relies on Scholander for allegedly teaching “coating heparin [an anticoagulant] on the membrane, heparin binds ionically with amino-groups on the surface - see col. 5, lines 30-67.” (Office Action at 3.) Scholander, however, fails to cure the deficiencies of Thomas, as discussed above. The Examiner does not provide any evidence that Scholander teaches an exchanger having a membrane coated with a layer of cationic polymer treated the membrane surface with a solution containing an anticoagulant agent, and subsequently purging the exchanger of the solution containing the anticoagulant agent prior to sterilizing the exchanger, as required by claim 26. Accordingly, Scholander certainly fails to teach “sterilizing the exchanger once the semipermeable membrane based on polyacrylonitrile carrying anionic or anionizable groups is coated with the cationic polymer and the anticoagulant agent,” (emphasis added) as recited in claim 26.

Accordingly, by combining the teachings of Thomas and Scholander, one skilled in the art would not have obtained the method recited in amended claim 26. Following the addition of a drop of cationic polymer on the membrane in Thomas (col. 5, lines 39-41), one skilled in the art would not have been motivated to subsequently treat the membrane surface in Thomas with an anticoagulant prior to sterilization. The purpose of adding only a drop of the polymer to the membrane surface during formation of the membrane in Thomas’s invention is to reduce the likelihood of damage to the membrane surface upon sterilization, which teaches away from Scholander’s teaching of coating a surface with an anticoagulant and subsequently sterilizing the membrane

after manufacture. The membrane surface in Thomas is only completely coated with the polymer after sterilization. Therefore, one skilled in the art would never even consider treating the membrane surface of Thomas, which contains a drop of a cationic polymer solution at one access, with an anticoagulant before sterilization. It would not have been feasible to obtain a membrane coated with a cationic polymer and an anticoagulant prior to sterilization, as recited in claim 26, by following the teachings of Thomas in view of Scholander at the time of the invention. Moreover, neither Thomas nor Scholander, or the combination of the two references, teaches or suggests purging the exchanger of a cationic polymer and anticoagulant coated on the membrane, prior to sterilization, as recited in amended claim 26.

Regarding the Examiner's assertion that "selecting or changing [the] order of process step[s] is prima facie obvious" (Office Action at 2-3), Applicants respectfully disagree that this statement and the cases the Examiner cites for support are relevant to this application, based in part on the complexity of the claimed process compared to those at issue in the cited cases. Applicants have shown, as discussed above, that the steps recited in claim 26 are not taught in Thomas or Scholander, or through a combination of those references. Moreover, the order of the steps recited in amended claim 26 provide a safe and ready-to-use exchanger. Additionally, the success of sterilizing a membrane already coated with a cationic polymer and an anticoagulant is unexpected based on the teachings of Thomas. In particular, Thomas even states that two additional stages would be necessary, one of which may "even [be] impossible to carry out, [and] it would be understood that adding four additional stages to an industrial manufacturing process would make its cost prohibitive." (Col. 8, lines 40-55.) Thus,

Thomas teaches that further steps would be required to even be potentially effective in preparing the membrane for sterilization if the cationic polymer was already coated on the membrane surface. Amended claim 26, on the other hand, provides a method for preparing a membrane coated with a cationic polymer and an anticoagulant that is subsequently sterilized, and does not require further steps as suggested by Thomas. Accordingly, the process of reducing the thrombogenic character of an exchanger by treating a membrane, as recited in claim 26, would have provided unexpected favorable results to one of skill in the art with knowledge of Thomas and Scholander.

Therefore, due to at least the deficiencies of Thomas and Scholander discussed above, amended claim 26 would not have been obvious to one of skill in the art at the time of the invention. Moreover, one of skill in the art would not have been motivated to combine Thomas and Scholander to obtain the invention recited in amended claim 26. Thus, amended claim 26 is allowable over the applied references, and claims 27-30 are allowable at least due to their dependence from amended claim 26.

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 26-30 in condition for allowance. Applicants submit that the proposed amendment of claim 26 does not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented new prior art references and some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the

entering of this Amendment would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the Amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

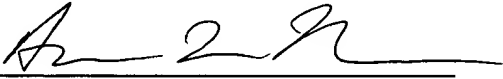
In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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